January 25, 1929. Vision of left eye practically 20/20. No central scotoma. Nose packed for the last time. Before patient was finally dismissed his vision had improved to 20/15.

* * *

CASE 2.—Mr. J. O. Age 64. A former patient, came in May 2, 1929, stating that the vision of the right eye had blurred the past two days.

Status.—The left eye was normal throughout.

Right eye.—Vision 20/100. Normal field, large central scotoma for white.

Right side of nose, which showed marked deviation of the septum, was packed with a tampon of adrenalin and ephedrine. Two days later the vision had dropped to less than 20/100. His nose was again packed. Two days later his vision had fallen to 10/100. The next day it was 5/100 in spite of repeated nasal tampons. On May 8, an operation was performed, straightening the septum and opening the ethmoids. Six days later the vision was 20/50, and two weeks later was up to his normal visual acuity, with no central scotoma.

RAYNAUD'S DISEASE—RECENT EXPERIMENTAL STUDIES*

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DISCUSSION *by C. Latimer Callander, M. D., San Francisco; Henry H. Lissner, M. D., Los Angeles; William H. Barrow, M. D., San Diego.*

DURING the past year work was undertaken, in collaboration with Sir Thomas Lewis,[1] to demonstrate the applicability of certain experimental methods of studying the blood supply of the human skin, to specific clinical problems. Raynaud's disease was chosen as the malady best suited to this purpose.

In this malady the digits become periodically pale or cyanotic, and, after several winters with repeated attacks, may show loss of tissue by a process of slow, dry gangrene. It is generally assumed that an obstruction of the blood flow to the digits underlies the condition; but the site of the obstruction, its nature, and the way it is brought about, has been open to debate.

Very little has been added to the admirable description of the visible phenomena since the publication of Raynaud's monographs in 1862 and in 1874; and it was thought that no point would be gained by proceeding further with the observational method. The experimental method was, therefore, employed to investigate the condition of the hands during the actual attacks, to discover the circumstances under which such attacks occur and subside, and to induce the attacks and analyze the various factors and the mechanism underlying them.

STUDIES ON TEMPERATURE SUITED TO ATTACK

In the beginning some difficulty was experienced in determining the temperature most suited to the production of an attack, the necessary time of exposure, and the temperature of the room necessary to maintain an attack. It was found that overcooling of the digits by immersion of the hands in cold water (5 to 10 degrees centigrade),† or exposing the hands to a low outdoor temperature through an aperture, with the patient remaining in a warm room, led to failure to induce attacks. Studies of the surface temperatures on the fingers of patients during attacks showed a range from about 15 to 18 degrees. Subsequently we were frequently able to bring on attacks indoors by immersing the hands in water at 15 degrees, for periods of ten to fifteen minutes, and in several cases over a very wide range of room temperatures. The reasons why overcooling by immersion fail are: (*a*) The minute vessels of the skin in these cases react as do those of normal skin to excessive cold (0 to 10 degrees) by dilating; and pallor tends not to occur, therefore. (*b*) Dissociation of oxyhemoglobin does not occur, or occurs only slowly at these temperatures; this hinders or prevents cyanosis. (*c*) Excessive cold (0 to 10 degrees) induces an after-reaction in the skin, tending to dilate the arterioles; this reaction, though far less free than in normal subjects, always happens, and, by establishing a flow of blood through the skin, maintains a healthy-looking color.

In carrying out our study, nine out of many patients examined were selected for more elaborate tests: three patients representing the more advanced stage with dry gangrene of one or more finger tips; two patients in an intermediate group; and four patients of the milder type, and without loss of tissue. The main part of our studies occupied the months from November 1928 to April 1929, and included a long period of very cold weather in London, extending from early in December to the first week of March.

Observations were made during a large number of attacks from their very beginnings, and many were induced under control conditions with the hands kept at rest. The onset, as indicated by color changes, usually took place within ten to fifteen minutes, at a room temperature of from 10 to 18 degrees. Immersion in water at 15 degrees was also usually successful in initiating attacks. In one case we were not successful in showing the influence of cold. Emotional factors may have played some rôle in bringing about variable results in this case.

Recovery from attacks begins with a restoration of normal color within a few minutes to an hour, if the room temperature is brought to 20 degrees or more.

In milder cases the recovery at ordinary room temperatures was often rapid, with at first an increase in the depth of the violet tint. Then a bright red spot or streak would appear near the base of a finger, rapidly spreading over the finger and persisting. The temperature of the skin soon began to rise, and within about twenty minutes was very much above room temperature. This indicates an increase in the circulation and flooding with fresh oxygenated blood of the fingers,

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† Temperatures throughout are in the centigrade scale.

due to release of preëxisting spasm of vessels. This reaction in the milder cases indicates the response to overcooling, which assumes importance when the question of therapy is considered.

In the severe cases the temperatures of the skin closely followed the temperatures of the surrounding air. Recovery in ordinary room temperatures was slower, and frequently progressed only partially, the skin becoming bright red or salmon color in patches near the bases of the fingers, and then gradually returning to the violet tint. This return to the cyanotic tint was more noticeable at lower temperatures. These minor stages of recovery frequently were unaccompanied by changes in temperature, and indicate the release of a very small trickle of arterial blood, which is not sufficient in amount to alter the temperature of the finger. A slight release of the spasm of the arterioles is sufficient to account for the change in color from violet to red; and the gradual return to the cyanotic tint is explained by the slow oxygen-carbon dioxid exchange at this temperature. The play of colors so often described in this disease is thus readily understood. It does not indicate that the vessels are completely released from spasm.

The reaction to overcooling has been previously mentioned. In the normal subject at moderate room temperatures, a finger which has been cooled in water at or near 0 degrees for five or ten minutes, withdrawn and gently wiped dry, subsequently shows a reaction, and becomes a good deal warmer than the adjoining fingers. This reaction is usually at its height in about fifteen or twenty minutes, and continues for an hour or more. Simultaneously, the skin of the cooled part becomes bright red. These changes are due to an increased circulation to the part. This protective mechanism is of great importance to the individual, and aids in his protection during cold weather.

In milder cases of Raynaud's disease, the reaction to overcooling approaches that seen in normal subjects; whereas, in the more advanced cases the reaction is very slight, or absent. The skin may become reddened; and this may persist for hours, but indicates only a slight vasodilatation. Repeated exposures of the finger or hand may maintain an improved circulation in the part and prevent attacks of cyanosis, as will be discussed later.

A test was employed to show the rate of blood flow of a small area of the skin. When immersed in water below 10 degrees or above 40, the skin becomes red. Between these temperatures there are normal variations from cyanosis (at 20 degrees), which gradually changes to red as the higher temperatures are reached (40 to 45 degrees). In the more severe cases of Raynaud's disease, the full cyanotic tint persists until the temperature of about 30 degrees is reached; and then there is a rapid change, approaching the color tints seen in the normal subject above this point. In milder cases the curves approach the normal. This indicates that the state of the vessels in these cases deviates but little from the normal, when the fingers are kept above the temperature necessary for the production of an attack. In the more severe cases the vessels remain in spasm until much higher temperatures are reached (25 to 30 degrees). At the higher temperatures (40 to 45 degrees), the vessels in the severe cases are capable of a nearly normal expansion.

STUDY OF BLOOD VESSEL INVOLVEMENT

Studies were made on the vessels involved in the spasm, their direct stimulation, and their capacity to dilate. It may be assumed that the circulation is stopped in the fingers during an attack of deep cyanosis or marked blanching. If the finger is cut it does not bleed. Numbness appears within fifteen or twenty minutes after the onset of the attack, indicating that the nutrition of the sensory nerve endings is impaired. If the skin of the finger is examined microscopically during an attack, it will be seen that the circulation has stopped in the small field examined. Obviously none of these tests of cessation of blood flow can be used practically and with sufficient accuracy for repeated observations. We have found the color scale,[2] where a tint XIV or XV indicates full cyanosis, and VI and VII a full hyperemia, to be a reliable guide. Full cyanosis develops after the circulation has been deliberately shut off to a part, and the fingers kept warm. It is essential that the skin be of good color, and the vessels full (as by reactive hyperemia) when the circulation is obstructed, as a pale tint is not readily determined. When the full cyanotic tint appears under test conditions, while the finger is cold (15 degrees), one can assume that the circulation to the part has stopped; and if such tints appear in a warm finger, it can be assumed that the circulation in it is greatly reduced.

In spontaneous attacks of cyanosis in Raynaud's disease, the discoloration appears first at the tips of the digits and moves toward their bases. During the stage of recovery the clearing-off process first manifests itself at the bases or along the sides of the proximal phalanges; and quickly or intermittently the fingers become a bright red color again.

It was abundantly shown that the veins of the hands and fingers play no part in the vascular spasm. There is free passage from the minute vessels of the skin to the main veins of the arm.

The radial artery or the other main arteries to the hand were not found to be directly concerned with causation of the attacks. The radial pulse could always be felt during attacks, although in some instances the entire hand was affected to the wrist. The radial pulse may be small; but this phenomenon is to be observed in normal persons when the hand is cold, and therefore lacks significance.

The actual site of the obstruction required further study. When the circulation to the fingers had ceased, in attacks, it was found that exposure to warmth by soaking the hand in hot water (40 to 45 degrees) would quickly restore the pink

or red color. If only the distal half or two-thirds of a finger, in attack, is exposed to hot water, there is only an increasing depth of color in the skin of the part submerged. There is only local dilatation of vessels; and there is no relief of the spasm which exists in the main digital arteries above the water line. If, however, the palm of the hand is warmed, including the bases of the fingers, the spasm of the vessels relaxes, and the color gradually returns to the finger as circulation is restored. There is evidence that the digital arteries, during an attack, are in spasm throughout their length. Smaller arteries or arterioles in the fingers and vessels of larger order and of the palmar arch, may also be simultaneously involved; but it is obvious that the chief fault does not reside in these vessels. There is also no evidence that a central reflex mechanism is active in the onset or offset of attacks.

Spasm has been produced by local cooling. In the case of fingers the area of cyanosis is less than the cooled part, indicating spasm of the deeper vessels, instead of spasm of the cutaneous branches. If some of the fingers and the corresponding side of the palm (*e. g.,* ulnar) are immersed, then the fingers show circulatory arrest in their whole length. Observations were facilitated by the use of a special tank in which the arm and hand could be cooled to any desired temperature (usually 10 to 15 degrees), and the fingers, which were passed through openings, protected by thin rubber membranes, could be maintained at a higher temperature (30 degrees) to determine the onset of cyanosis. It was found that if the fingers were kept at lower temperatures (10 to 15 degrees), the appearance time of cyanosis was delayed because of the slow, gaseous exchange. Furthermore, the degree of cyanosis was more difficult to evaluate when the skin was pale. It was necessary to cool the hand to the bases of the fingers, while the fingers beyond this point were kept warm (at 30 degrees) for the reason stated above, to bring on attacks of cyanosis—again showing that the digital arteries at their origins in the palm are closed by spasm under the conditions of cooling.

Another test which was devised showed that the palmar vessels near the bases of the fingers must be cooled to bring on attacks in the entire finger. A stream of cold water (at 10 degrees) was passed through a flat lead box, resting on the palm of the hand to the bases of the fingers. The hand was submerged in a warm bath at 30 degrees. After fifteen or more minutes, attacks could be produced if the box was properly located to include the bases of the fingers. By proper adjustment, a single finger could be put into attack. Recovery took place by passing warm water through the box, or immersing the palm in warm water after the box was removed. Another method of inducing spasm in a single finger was used in the more severe cases. A brass capsule with thin, perforated rubber membranes at each end was placed on the finger; and water at 10 degrees passed through it while the hand was submerged in a bath at 30 degrees. By this method, cyanosis would be produced in the last phalanx, and recovery take place when warm water was again passed through the capsule. These observations show that different parts of the digital vessels are equally acted upon by the cold stimulus. They are of great importance when one considers the conditions of exposure of patients suffering from this malady. The fingers are of smallest circumference, and quickly lose heat at lower temperatures. The vessels contract, and the effects are first manifested at the finger tips, gradually moving toward the bases of the fingers. If the exposure is long enough the vessels in the palms are likewise sent into spasm. Further exposure may affect the vessels of the entire hand, or, in some instances, may advance to even larger vessels in the arm.

There is no conclusive evidence that vascular spasm in these cases is a local vasomotor phenomenon. The effects of direct stimulation of the vasoconstrictor fibers and reflex vasomotor impulses are conveyed widely. The theory of a reflex mechanism responsible for the local changes presupposes a complex system of selective areas in the central nervous system which is not supported by any direct evidence. One can only conclude that the peripheral vessels in these cases are hypersensitive to local cooling and that the central nervous system takes no part in the reaction.

Experiments were devised to show whether the changes in the vessels were due to spasm alone or whether the vessels were principally the site of structural changes. Studies on pulse volume showed that in the milder cases the vessels were quite capable of expansion as the temperatures were increased. In the more severe cases, with loss of substance, the vessels were less readily opened by increasing increments of heat; but were almost as widely dilated at higher temperatures (from 40 to 45 degrees), as were normal vessels. There was very little circulation to the fingers until a temperature of about 30 degrees was reached, which corresponds to the changes in color which were found to occur at about the same point. It is obvious that the loss of substance in these cases at the tips of the fingers is secondary to long-sustained arrest of circulation in these parts. At ordinary room temperatures (under 30 degrees) the vessels are incapable of more than partial relaxation.

There was not enough evidence in our patients to show that the small superficial vessels in other parts of the body were sufficiently involved to lead to serious results. In patients where local necrosis has occurred at the tip of the nose or the tips of the ears or elsewhere, it may be assumed that the local vessels are also at fault.

It is well known that the depth of color in the fingers during attacks varies from a pale, waxy color to a deep violet tint. We were able to show that the depth of tint depended upon the amount of blood in the minute vessels at the time of onset of the attacks. Too much attention has been given to the symptom of pallor. It has no great significance, and is not an essential phase of the phenomena of attacks. In no instance where the

attacks were observed from their onset, either spontaneously or experimentally induced, was the waxy or so-called "dead white finger" observed. This phase is artificial, and brought about by involuntary movements of the fingers during the onset of attacks, when the fingers are rubbed at the first appearance of sensation of cold in the parts; when tight gloves are worn; or under similar conditions which may remove the blood from the periphery. The original statement of Raynaud, which has since been frequently repeated in the literature, that the colors observed during an attack are at first white, then blue, and finally red in the stage of recovery, needs revision. The white stage is entirely artificial.

When blanching occurred in the affected parts, the minute vessels were shown to be in a state of contraction. Increase of venous pressure in the arm to 40 millimeters Hg produced cyanosis in the extremity to the areas of blanching. These slowly cleared if the pressure was maintained. If at any stage the pressure was released, the remaining blanched areas tended to remain so; and the hand on the opposite side continued in the blanched state. It would be difficult to explain these phenomena on the basis of central or vasomotor influences. The appearance of Bier's spots or local areas of blanching of skin, strongly suggest local spasm in smaller vessels. They appear in skin which has been deprived of all nerve supply.

STUDY OF INFLUENCE OF VASOMOTOR NERVES

Much is being written on the influence of vasomotor nerves upon spasm of the peripheral arteries in this and other diseases. There is no direct evidence that the vasoconstrictor impulses exert more than a tonic effect upon the muscles of the arterioles. While an interruption of the central impulses may remove to some degree the tone of the vessels, and does so in the normal individual, there is insufficient proof that it is a major factor in causing the symptoms of Raynaud's disease. Published reports on ramisection and ganglionectomy are inconclusive on this point. By relaxing the tone of the vessels the circulation to the part may be improved, and the resultant temperature may be elevated, requiring a greater amount of cooling to give local spasm of the vessels.

On several occasions we resorted to local anesthetization of the ulnar nerve during attacks. With the skin completely anesthetized over the area of ulnar distribution and the corresponding area of vasomotor dilatation outlined by hyperemia and other local effects—dryness, increased temperature, etc.—it was possible to initiate characteristic attacks by suitable methods. It may be assumed that the vasoconstrictor nerves pass to the extremity with the mixed nerves, and that they have no connections of any length in the sheaths of the vessels themselves.

These points, however, are not advanced as an argument against the practical value of ramisection, particularly in mild cases, as the removal of vasomotor tone might compensate for a partial loss of the local reflex mechanism.

On theoretical grounds it appears unlikely that all the possible vasoconstrictor connections to the brachial plexus should be severed to bring about vasomotor paralysis to the arm. One would not expect that the lesser connections through the first and second dorsal nerves would exert any great tonic action on the state of the vessels of the entire arm and hand. The proponents of such extensive surgical procedures have been swayed by the almost universal acceptance of Raynaud's view that the spasm of the vessels was due to nervous influences. One cannot state that the vasomotor influence can be ignored in considering this disease. Given proper conditions, the central impulses may turn the balance to decide the resultant effects in the extremities. This may be shown by experiments conducted in rooms of different temperatures. When attacks cannot be brought on in rooms at high temperatures, they may then occur if the room temperature is greatly reduced. The same results may be obtained if severe pain is produced. There is no direct evidence that this influence is any greater in a patient with Raynaud's disease than in the normal individual. Our view is that the defect in these cases is a local one, as has been amply demonstrated. The confusion which has existed from Raynaud's time respecting the vasomotor influences has been largely due to the inclusion of patients with general nervous phenomena in the group classified as "Raynaud's disease." We described one such case. We were unable to find any evidence of spasm in the retinal vessels, which is described in the literature, in this or in our other patients.

Before much further advance is made in the knowledge of this disease, it is necessary to carefully segregate the different types now vaguely classified as Raynaud's disease. In the type we describe, the condition of the digital arteries is peculiar. They show a direct reaction to low temperatures, with spasm accompanied by discoloration; and, eventually, nutritional changes appear in them. The relationship with local or general scleroderma and with local arthritic changes is not entirely clear, but it may be surmised that these latter conditions are secondary.

SUGGESTIONS FOR TREATMENT

Suggestions for treatment may be premature at this time. However, observations resulting from overcooling in the normal and in the group of cases studied are of interest. Our early failure to provoke attacks was due to a lack of appreciation of the mechanism of this reaction in our cases. In the normal individual an exposure to temperatures of from 0 to 10 degrees for several minutes results in a reaction which increases the circulation of the cooled part, and a consequent elevation of the temperature above that of the uncooled areas. This appears to be a normal biological protective mechanism. In the milder cases, without loss of tissue, the mechanism is but slightly altered, but in the advanced cases, with local necrosis, there is little or no reaction to overcooling. The color may become red, but the tem-

perature of the skin follows closely the room temperature. The normal reaction persists for an hour or more, with the part at rest, but may be more prolonged if the individual is actively moving about. In one of our more severe cases the circulation in one hand seemed improved over its fellow during repeated exposure, and persisted after the treatment was stopped. In another instance the treatment was discontinued because of pain accompanying the treatment.

Since our observations were published, the author has had an opportunity to study other patients showing milder degrees of severity, where one might expect to obtain better results from treatment. In them exposure of one hand to temperatures between 4 and 10 degrees would keep this hand red and warm and free from attacks, whereas the untreated control hand would show repeated attacks. It would seem advisable to avoid pain if the patient is to coöperate in treatment. The treatments should probably be given two or three times a day. They may at first be given and followed by gently warming the part in water or by placing the hand against a warm part of the body. Showers or tub baths with water at gradually lower temperatures may also be instituted.

SUGGESTED PLAN OF TREATMENT

A suggested plan of treatment is as follows:

First Week.—One hand or foot, preferably the one more seriously affected (companion as control), immersed in water at 10 degrees centigrade three times a day for ten minutes. Severe pain or faintness to shorten period of exposure, or time for reducing temperature.

Second Week.—Temperature reduced to eight degrees.

Third Week.—Temperature reduced to six degrees.

Fourth Week.—Temperature reduced to five degrees.

Fifth Week and Thereafter.—Temperature reduced to four degrees.

It is to be understood that this outline is merely suggestive. When quite certain that beneficial results are being obtained, shower or tub baths of decreasing temperatures may be instituted. If possible, treatments should be started before cold weather begins. The effects of the reëducation of the reaction to cooling may be studied, by following the surface temperatures, with the thermocouple under control conditions. Contrast baths may be used at first if desired.

Results of treatment in patients with Raynaud's disease, scleroderma and hypertrophic arthritis suggest that the principles outlined above may have a wide application. This method may also be used in the treatment of chilblains. The value of the empirical use of cold baths in the prevention of the common cold may well be due to the stimulation of this reaction as a protective mechanism against cold. The common cold may be found to be primarily a failure of this mechanism. Studies with this possibility in mind are being undertaken.

SUMMARY

A variety of Raynaud's disease has been studied. It is the form in which the digits become periodically pale or cyanotic, and in which, after several or many winters of repeated attacks, terminal portions of the digits may be lost by a process of slow, dry gangrene.

The circumstances in which attacks appear and disappear have been carefully observed. In mild cases there is but slight variation from the normal; but in severe cases the fingers slavishly follow the environmental temperature. These fingers do not react to overcooling as readily as do normal fingers, and are the ones which develop local gangrene.

The immediate cause of the defective circulation is spasm of the digital arteries. These vessels in the milder cases are capable of full expansion, and nearly so in the severe cases.

The meaning of the various discolorations, cyanosis, pallor, reddening that are displayed is discussed.

Local applications of heat and cold show that the spasm is profoundly influenced by temperature, in response to which the vessels behave abnormally. These observations are contrary to what would be expected if the current views ascribing the spasm to vasomotor influences were true; the abnormal element in the reaction to cold is a direct reaction, and is due to a peculiar condition of the vessel wall locally; it is not the result of a reflex action through the vasomotor nerves. The state of vasomotor nerves naturally influences the tone of the vessels in these patients, as it does in normal people; but the pathological element in the vascular spasm is not of central nervous origin, as at present it is generally thought to be. The effects of interfering with the nerves to the affected parts, by local anesthesia or by surgical division, are briefly discussed.

Suggestions for a rational treatment are given on the basis of original observation, and results achieved on a limited number of cases are mentioned. Further studies are being made in this direction. Certain frequently associated conditions are mentioned, and the application of this method of treatment to these and other disorders is proposed.

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DISCUSSION

C. LATIMER CALLANDER, M. D. (450 Sutter Street, San Francisco).—Much that is commendable might be said about many of the phases of Doctor Kerr's

work as outlined in this splendid paper. To a few points I would like to draw attention.

Doctors Kerr and Lewis, like so many English investigators, have utilized simple apparatus and easily controlled methods in the pursuance of their problem. Furthermore, they have chosen for their work Raynaud's disease, for which they had plenty of clinical material available. In London, where the weather is severe, there must be many more cases at hand and their symptoms must be more pronounced than occurs in California, where a true Raynaud's syndrome, in my experience, is unusual.

It is interesting that these investigators have spent little time discussing the so-called ischemic stage in this condition (pallor symptom). It seems reasonable that this is a phenomenon secondary to rubbing and clenching of the parts in an effort to lessen the discomfort. It is rare to see Raynaud's disease where the ischemic stage is a significant sign.

Doctor Kerr has noted only a slight hyperthermic reaction to overcooling in advanced cases, while he finds a very definite increase in temperature in the early cases. We have noticed that the affected extremities of patients with advanced Raynaud's disease become less hyperemic after the immersion of the part into the cold water of the contrast bath than is manifested in patients in the early stages of the lesion.

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HENRY H. LISSNER, M. D. (Roosevelt Building, Los Angeles).—In reading Doctor Kerr's paper on Raynaud's disease one is impressed by the careful experimental methods employed and their easy application to the clinical phenomena of the disease.

For many years investigators have discussed the pathologico-anatomical situation of Raynaud's syndrome, and while there is much to be said in favor of arterial disease in the experimental data presented, sufficient evidence is not available to justify the conclusion of definite arterial change to the exclusion of the vasomotor influence, especially that of a sympatheticotonia.

A sympathetic nervous system imbalance from the standpoint of the vasomotor control is evidenced in many conditions which, while they are allied or considered with Raynaud's disease, do not present the same clinical picture. Demographia, erythromelalgia, scleroderma, arthritic changes, and blushing or paling in their physiological aspects seem to bear a definite relationship to some of the clinical phenomena found in sympathetic imbalance. Just as every allergic reaction does not produce asthma but may cause numerous other manifestations in various organs of the body, so vasomotor disturbances need not always work on the terminal arteries causing the Raynaud's syndrome.

When one considers the frequency of arterial disease met with in the ordinary course of the practice of clinical medicine, and the infrequency of the occurrence of Raynaud's disease associated with it, the question of climatic conditions, *i. e.*, continued cold or rapidly changing temperatures, must be considered to play an important etiological rôle through the nervous regulatory mechanism for the control or maintenance of the normal heat regulation.

As a matter of fact, Doctor Kerr admits in his experiments that exposure of normals does show that a nervous mechanism controls the arteries and argues that "The vessels were less readily opened by increasing increments of heat, but were almost as widely dilated at higher temperatures (from 40 to 45 degrees) as were normal vessels." From this observation it may be deduced that the spasm is not relieved as readily under the influence of an unstable nervous system as in a stable one, since the end result is a vessel of the same size in disease as in the normal, with practically the same reaction.

The theory that a lesion of the peripheral arteries may account for the symptoms of Raynaud's disease finds many supporters. Certain anatomical findings have been cited as strong arguments by those who believe such lesions to be irrefutable evidence as opposed to pure theory.

Up to the present time, reported organic alterations in the vessels will not suffice to explain the symptoms any more satisfactorily than the theory of a central nerve affection of the sympathetic system.

Until more experimental data are offered which will more definitely remove this question from the realm of hypothesis, and which will consider intrinsic and extrinsic etiological factors, I will retain the opinion that sympatheticotonia has a great influence on the causation of Raynaud's disease.

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WILLIAM H. BARROW, M. D. (1400 Medico-Dental Building, San Diego).—The painstaking and carefully controlled experimental work on the effects of heat and cold stimuli in Raynaud's disease as reported by Doctor Kerr in this paper is an interesting and valuable contribution to the literature on the subject. It has been generally accepted in the past that Raynaud's disease was a manifestation of a "neurovascular diathesis" due to a sympathetic nervous system imbalance on perhaps a "neuro-endocrine basis." It has been felt that angioneurotic edema, scleroderma, intermittent claudication, erythromelalgia, certain forms of arthritis and other "vasomotor-trophic" disorders were closely allied etiologically. It has been recognized for some time that in the advanced cases of Raynaud's there were capillary changes and deformities, but it has also been believed that the disease was a generalized disorder and not due purely to local changes in the vessel walls as is Doctor Kerr's conclusion.

I saw recently a patient with Raynaud's disease, her symptoms and physical findings fitting the description of the disease as given by Doctor Kerr. I am reporting the case because it presents manifestations of the disorder which it would seem can only be explained on the basis of a generalized sympathetic nervous system imbalance. It is of interest that this patient's symptoms appeared with a change of environmental factors that subjected her to considerable psychic stress, and she reported that she was worse at times of particular nervous tension. She was subject to attacks of paroxysmal hematuria, having been cystoscoped at one time for this symptom with negative findings. She had had attacks of acute abdominal pain not entirely relieved by an operation for postoperative adhesions, and best explained perhaps by spasm of abdominal vessels. Her hands and feet were involved, the latter showing impending gangrene. At the time of her attacks of local syncope the radials were small in volume and the dorsalis pedis arteries did not have a palpable pulsation. This patient's feet often presented a waxy pallor of the distal parts, or of one or more toes or of disseminated patches when they had not been rubbed or manipulated or constricted. Usual medical measures, such as contrast baths, woolen stockings, local applications, massage, and sedatives, failing to give relief, she submitted to bilateral lumbar and later cervicothoracic ganglionectomies with a resultant restoration of normal circulation in her extremities. She has, however, had a recurrence of the hematuria and the abdominal pain. This patient was and still is subject also to attacks of angioneurotic edema.

Rountree and Ghrist recently reported some interesting observations on surface temperatures in normal subjects and in subjects with peripheral vascular disturbances as affected by the oral ingestion of ice water, indicating definite changes associated with the "pressor response to stimulation of the sympathetic nervous system," which response was, of course, no longer in evidence after ganglion resection.

In contradistinction to the suggestion in this work and in the case reported of the generalized nature of the vasomotor disturbance, an interesting case was recently reported by Cotton and Berg of a laundry worker who developed typical symptoms of Ray-

naud's disease in the thumb and index finger of the right hand, which had been traumatized by the constant sticking of pins into shirts over a period of years. Earlier involvement of fingers of the other hand indicated that the disease was a true Raynaud's and not a traumatic angitis. But the trauma had undoubtedly precipitated the manifestation of the disease in this part. Incidentally, this patient was relieved by vaccine shock. She also was reported as showing evidence of sympathetic instability, with a history of "goiter," and an exaggeration of the vasomotor as well as the deep reflexes.

It would seem that there may well be in this condition a combination of a central vasomotor imbalance with pathological changes in the peripheral vessels, the one reacting on the other. Such a combination probably exists in essential hypertension and is certainly possible in Raynaud's disease. The significance of the original work done by Doctors Kerr and Lewis cannot be denied, but there are certain clinical and experimental observations which do not seem to be clearly correlated with their hypothesis that the disorder is due entirely to a peculiar local condition of the peripheral vessel walls which causes the abnormal reaction to cold.

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Doctor Kerr (Closing).—There is very little to add to what has already been presented in the body of this report. It is not the intention of the author to imply that there is any pathological lesion in the peripheral vessels in Raynaud's disease. The disturbance is essentially a physiological one which, if continued, will eventually result in local gangrene of the tips of the extremities. The vasoconstrictor impulses apparently act in maintaining the tone of the peripheral vessels, but play no rôle in the production of phenomena which we group under the term of "Raynaud's disease."

DIVERSION OF THE URINARY STREAM BY URETERAL TRANSPLANTATION—ITS INDICATIONS AND ULTIMATE RESULTS*

REPORT OF CASES

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DIVERSION of the urinary stream by transplantation of the ureters into the skin, intestines, vagina, or urethra in incurable congenital and acquired malformations and lesions of the bladder relieves the inexpressible misery that these patients suffer, alleviates symptoms, lessens invalidism, and prolongs life. Unfortunately, the operation of ureteral transplantation is not performed early enough and these patients become progressively worse and finally die, not from the original bladder lesion, but from urinary stasis, sepsis, and uremia.

The indications for ureteral transplantation are extrophy of the bladder, extensive incurable bladder fistulae, malignant growths of the bladder and female adnexa involving the ureters, causing strangulation, incurable tuberculosis of the bladder, and incurable interstitial cystitis with formation of ulcers described by Hunner. Ureteral transplantation should only be performed as a last resort when all other therapeutic and surgical methods have failed to relieve the pathological lesion of the bladder or uterus. The patient is often a poor risk, having been weakened by months or years of suffering and by toxemia, and debilitated by lowered kidney function due to back pressure. Ureteral transplantation into the urethra and vagina is impractical in most cases because of the impossibility of securing a stump of sufficient length. The perfected operation of transplantation into the sigmoid gives excellent results, but is too extensive in extremely debilitated patients and still carries a high mortality. It is ideal for those patients suffering from extrophy in whom there were usually few renal complications. Transplantation of the ureters into the skin of the lower abdomen is simple, rapid and benign, and is an operation devoid of shock, which is well supported even by cachetic and debilitated persons. It also has the advantage of allowing for recognizing, studying, and caring for subsequent renal complications.

HISTORICAL NOTE

In 1869 Simon[1] accidentally cut the left ureter during the operation of ovariotomy and fixed the ureter to the skin of the abdominal wall. Later, in order to relieve the resultant fistulae, he performed a nephrectomy. Deliberate transplantation of the ureter into the skin was proposed by Hayes-Agnew[2] in 1881 and performed for the first time by Laurenze[3] in Rome in 1888, but the details of the operation and the clinical course of the patient are lacking. In 1889 Le Dentu[4] purposely implanted the ureter into the skin of a patient suffering from metastases of a cancer of the uterus which had involved the left ureter, and which had caused anuria of seven days' duration. The operation was successful inasmuch as the patient was relieved from urinary back pressure, but death occurred some thirteen days later from generalized carcinomatosis. Two years later Pozzi[5] accidentally severed the ureter in removing an enlarged, adherent pelvic tumor. He transplanted the ureter into the skin of the lumbar region, but performed a nephrectomy some three months later to relieve the urinary fistula. The kidney in question was carefully studied by Albarrán,[6] who noted that the organ was very little damaged, presenting only the phenomena of slight back pressure and a mild degree of pyelonephritis and very slight alteration of the parenchyma. The operation was later performed for incurable bladder lesions by Albarrán,[6] Giordano,[7] Zuckerkandl,[8] and Frank.[9] Legueu and Papin[10] made numerous experiments on animals and cadavers in order to perfect the operation and made a detailed report in 1921, including nine ureterostomies on human beings. Following this, successful results were obtained by Huc,[11] Duvergey,[12] Day,[13] Rosenkranz,[14] and Ormond.[15] In 1925 I had the privilege of hearing Papin[16] de-

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